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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/527,430	03/09/2005	Jeffery A Bibbs	DIAKR.007NP	5428

20995 7590 02/05/2010

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EXAMINER	
BETTON, TIMOTHY E	

ART UNIT	PAPER NUMBER
1627	

NOTIFICATION DATE	DELIVERY MODE
02/05/2010	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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Office Action Summary	Application No.	Applicant(s)	
	10/527,430	BIBBS, JEFFERY A	
	Examiner	Art Unit	
	TIMOTHY E. BETTON	1617	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *05 January 2010*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,2,4,5 and 7-11* is/are pending in the application.

4a) Of the above claim(s) *7-11* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,2,4 and 5* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Applicants' Remarks filed on 5 January 2010 have been acknowledged and duly made of record.

Status of the Claims

Claims 1, 2, 4, and 5 are pending further prosecution on the merits. Claims 7-11 are withdrawn from further consideration.

Response to Arguments

Applicants' argue the rejection under 35 U.S.C. § 102(b) over anticipation. Applicants' arguments are considered and are found persuasive. The rejection under 35 U.S.C. § 102(b) is hereby withdrawn.

Applicants' assert comments concerning the rejection under 35 U.S.C. § 103 (a) over obviousness. However, through out pages 15-18, applicants' fail to show factual/substantial evidence to the contrary as regarding the Examiner rejecting claims 1, 2, 4, and 5 under 35 U.S.C § 103(a) as being unpatentable over Kumar in view of Kobrin et al. *(Safety of Mibefradil, a New Once-A-Day, Selective T-Type Calcium Channel Antagonist,* The American Journal of Cardiology, Vol. 80 [48], 1997, printed pages 1-7) ("Kobrin") and U.S. Patent Publication No. 2001/0049447 to Li et al. ("Li").

Applicants' disagree and through out said pages 15-18, there is only disagreeable language but no substantial evidence proving nonobviousness over the references cited in the current 103(a) of record. Applicants' do not clearly address why the references *supra* in the said 103(a) are not obvious.

Thus, for the reasons already made of record, the rejection under 35 U.S.C. § 103 (a) over obviousness is maintained.

Rejections not reiterated from previous Office Actions are hereby withdrawn. The following rejections are either reiterated or newly applied. They constitute the complete set presently being applied to the instant application.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1, 2, 4, and 5 are rejected on the ground of nonstatutory double patenting over claims 50-52 of U. S. Patent No. 6,852,742 B2 since the claims, if allowed, would improperly extend the "right to exclude" already granted in the patent.

The subject matter claimed in the instant application is fully disclosed in the patent and is covered by the patent since the patent and the application are claiming common subject matter, as follows: Column 76 at lines 33-44 9 (claims 50-52) disclose

50) A method of treating a disease associated with a cellular calcium channel comprising:

a) Identifying a subject in need of such treatment

b) Administering to said subject an effective calcium-channel antagonizing amount of a compound of claim 1, wherein said disease is a cardiovascular disease or neurological disorder.

51) The method of claim 50, wherein said subject is a mammal.

52) The method of claim 51, wherein said subject is a human.

Claims 1, 2, 4 and 5 of the current invention essentially teach a species of a disease associated with a cellular calcium channel in that claim 1 teaches a method for inhibiting calcium T-channel activity via a calcium channel antagonist specific for T-channel activity.

Specifically, claim 2 is encompassed by prong b) of patented claim 50) because of the disclosure drawn to administering to said subject an effective calcium-channel antagonizing amount of a compound. Further patented claims 51 and 52 are likewise encompassed by the limitation in prong b) by teaching a subject in need thereof which constitutes a human being and mammal.

Furthermore, there is no apparent reason why applicant was prevented from presenting claims corresponding to those of the instant application during prosecution of the application which matured into a patent. See *In re Schneller*, 397 F.2d 350, 158 USPQ 210 (CCPA 1968). See also MPEP § 804.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 1, 2 4, and 5 are rejected under 35 U.S.C. 103(a) as being unpatentable over Pullela et al. (USPN 6,852,742).

Column 76 at lines 33-44 9 (claims 50-52) of Pullela et al. disclose

50) A method of treating a disease associated with a cellular calcium channel comprising:

a) Identifying a subject in need of such treatment

b) Administering to said subject an effective calcium-channel antagonizing amount of a compound of claim 1, wherein said disease is a cardiovascular disease or neurological disorder.

51) The method of claim 50, wherein said subject is a mammal.

52) The method of claim 51, wherein said subject is a human.

Claims 1, 2, 4 and 5 of the current invention essentially teach a species of a disease associated with a cellular calcium channel in that claim 1 teaches a method for inhibiting calcium T-channel activity via a calcium channel antagonist specific for T-channel activity.

Specifically, claim 2 is encompassed by prong b) of patented claim 50) because of the disclosure drawn to administering to said subject an effective calcium-channel antagonizing amount of a compound. Further patented claims 51 and 52 are likewise encompassed by the limitation in prong b) by teaching a subject in need thereof which constitutes a human being and mammal.

Pullela et al. does not teach a method for inhibiting calcium T-channel activity explicitly.

However, it would have been *prima facie* obvious to the one of skill at the time of invention to administer the title compound I (see column 68 at lines 47-57) for the treatment of a disease associated with a cellular calcium channel as taught by Pullela et al. This particular disease as taught by Pullela et al. fully encompasses the species disclosed in claim 1 of the claimed invention.

The motivation to employ Pullela et al. in obviousness over the claimed invention is drawn to Pullela et al. teaching the same antagonist as a compound of Formula I for the treatment of a disease associated with a cellular calcium channel which reasonably encompasses in obviousness the limitation in the current claim drawn to selectively inhibiting calcium T-channel activity.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1, 2, 4, and 5 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kumar et al. (Synthesis and Evaluation of a New Class of Nifedipine Analogs with T-Type Calcium Channel Blocking Activity, Mol. Pharmacol. 61: 649-658, 2002 in view of Kobrin et al. (Safety of Mibefradil, a New Once-A-Day, Selective T-Type Calcium Channel Antagonist, The American Journal of Cardiology, Vol. 80 [48], 1997, printed pages 1-7) in view of Li et al. (USPGPUB 2001/0049447 A1).

For the reasons already disclosed above, Kumar et al. is reapplied in obviousness over claimed invention.

Additionally, Kumar et al. teach the similarities with regard to mechanisms of action with the compound as elected and the drug, Nifedipine (page 654, col. 2, page 655, 1st col., 1st paragraph).

Kumar et al. does not teach "prodrug".

However, Li et al. resolves the deficiency of Kumar et al. in view of the limitations contained in the current invention by teaching [...] prodrugs, the compounds of the present invention may additionally or alternatively be prepared to be delivered in a prodrug form. The term prodrug indicates a therapeutic agent that is prepared in an inactive form that is converted to an active form (i.e., drug) within the body or cells thereof by the action of endogenous enzymes or other chemicals and/or conditions [0021].

Li et al. teach embodiments replete with T-type channel antagonist such as nifedipine which was indicated in Kumar et al. as having similar P450 inhibition profile and mechanisms of action as the elected compound.

Li et al. does not teach once a day dosing of a T-Type channel antagonist.

However, Kobrin et al. resolves the deficiency in Li et al. by teaching the once a day dosing of Mibefradil, a conventional T- Type channel antagonists. Further, Kobrin et al. disclose methods which include nifedipine which was indicated in Kumar et al. as having the same affinity toward the same receptors as the chemical moiety as elected (PPK-5 in the Kumar reference) (please see Methods, 2nd column, 1st full paragraph).

Thus, it would have been prima facie obvious to the one of skill at the time of invention to recognize a reasonable expectation of success via the combining the incorporating together the teachings and methods of Kumar et al., Li et al. and Kobrin et al.

In determining the scope and content of the prior art, Kumar et al. adequately teach subject matter which is obvious over the claimed invention. Kumar et al. teach the elected moiety disclosed as PPK-5, which is similar in activity to nifedipine (a well-known selective inhibitor). Li et al. teach T-Type channel antagonists as prodrugs which makes claim 4 obvious. Kobrin et al. teach a pharmaceutical composition comprising an art-known T-type inhibitors such as Mibefradil and nifedipine which are indicated in a regimen for once-a-day administration.

In view of the teachings of Kumar et al., the said reference clearly teaches the similarities of nifedipine with regard to the elected species. The elected compound is taught expressly throughout the Kumar et al. reference. However, agents such as nifedipine are further elucidated with reference to clear therapeutic regimens. This is the ascertained difference between the prior art and the claims at issue.

In considering objective evidence present in the application indicating obviousness, the one of skill would readily be inclined to recognize that if nifedipine and Mibefradil exemplify

the same mechanisms of action as the elected compound and/ or vice-versa, then the claimed invention is thus overcome by obviousness in the teachings and methods of the references disclosed *supra.*

With regard to the limitation "in regular doses no more often than once per day", the MPEP cites thus:

I. SOMETHING WHICH IS OLD DOES NOT BECOME PATENTABLE

UPON THE DIS-COVERY OF A NEW PROPERTY

"[T]he discovery of a previously unappreciated property of a prior art composition, or of a scientific explanation for the prior art's functioning, does not render the old composition patentably new to the discoverer." Atlas Powder Co. v. Ireco Inc., 190 F.3d 1342,1347, 51 USPQ2d 1943, 1947 (Fed. Cir. 1999). **Thus the claiming of a new use, new function or unknown property which is inherently present in the prior art does not necessarily make the claim patentable.** In re Best, 562 F.2d 1252, 1254, 195 USPQ 430, 433 (CCPA 1977). >In In re Crish, 393 F.3d 1253, 1258, 73 USPQ2d 1364, 1368 (Fed. Cir. 2004), […].**The court stated that "just as the discovery of properties of a known material does not make it novel, the identification and characterization of a prior art material also does not make it novel."** Id.< See also MPEP § 2112.01 with regard to inherency and product-by-process claims and MPEP § 2141.02 with regard to inherency and rejections under 35 U.S.C. 103.

Thus, the limitation "in regular doses no more often than once per day" is an inherent use of any pharmaceutical composition administered by mouth to a patient in need of such treatment. It would be instantly apparent to the one of skill in the pertinent art that a T-channel agonist oral composition would be given *at least* once per day which reasonably encompasses in obviousness

over the limitation of the current invention which discloses "in regular doses no more often than once per day".

Further, absent of any indication in the specification with regard to what is meant by the term "regular", the said term is given its broadest interpretation in view of the scope of the claimed invention. In this said case, a regular dose would be characterized as a concentration sufficient to affect a physiological change in a mammal body. Kumar et al. as a result fully anticipates the claimed invention by teaching a concentration ranging from 0.3 μM-3 μM of PPK-5 on transiently expressed on T-type channels obtained from 11 different cells (please see Figure 6, graphs A and B).

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Timothy E. Betton whose telephone number is (571) 272-9922. The Examiner can normally be reached on Monday-Friday 8:30a - 5:00p.
If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreeni Padmanabhan can be reached on (571) 272-0629. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access

to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/SREENI PADMANABHAN/

Supervisory Patent Examiner, Art Unit 1627